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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,876	11/28/2000	Bryan Julien	300622003110	7402

7590 04/02/2004

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EXAMINER

NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	Application No. 09/724,876	Applicant(s) JULIEN ET AL.	
	Examiner Nashaat T. Nashed, Ph. D.	Art Unit 1652	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 22 September 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 29-44.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_



Nashaat T. Nashed, Ph. D.  
Primary Examiner  
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Claims 29-44 are under consideration.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 29-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schupp *et al.* (Schupp, IDS paper number 11, Ref.No. 11: U. S. Patent 6,121,029) in view Khosla *et al.* (Khosla A, U. S. Patent 6,391,594) and Khosla *et al.* (Khosla B, IDS paper number 11, Ref No. 33: WO 97/02358) for the reasons set forth in rejecting original claims 15-17 and 24 in the prior Office actions mailed 11/12/02 and 5/21/03.

In response to the above rejections, Applicants argue that since Schupp *et al.* do teach that a non-epothilone gene cluster methyltransferase gene is required to place the C-12 methyl in epothilone and fail to mention epothilone C or D in the specification.

Applicants' arguments filed 9/22/03 have been fully considered but they are not deemed to be persuasive. The pending claims are not limited to a specific modification or a composition of proteins, which would synthesize a specific chemical compound. The claims are directed to any modification in any of the  $\beta$ -carbonyl modifying activity encoded by a *Sorangium cellulosum* of epoD modules 4-6. The modification could be deletion or substitution by any other from any other PKS. The examiner agrees with the applicants that Schupp *et al.* does not teach modified epoD as evidenced by the fact the rejection is made under 35 U.S.C. 103(a) and not under 35 U.S.C. 102, but they teach the gene cluster which produces epothilone A and B. Epothilone C and D are precursor to epothilone A and B, respectively, and therefore, Schupp *et al.* have taught all the gene required for the biosynthesis epothilone A, B, C, and D. As indicated in the prior Office action, Schupp *et al.* and Khosla A provide one of ordinary skill in the art with motivation and expectation of success to make derivatives of epothilone which would be very difficult to obtain by organic synthesis. Working with DEBS gene cluster, Khosla *et al.* reported several new compounds obtained from deleting and substituting KR2. The claimed modified epoD have not produced any unexpected result or compounds that would have not been expected from the teachings of gene cluster of epothilone taught by Schupp *et al.* and the teaching of modifying various activities of similar PKS from the DEBS gene cluster. While the amended claims are narrower in scope than the previously rejected claims, they are drawn to non-specific modifications, which are obvious over the prior art of record. Regarding applicants argument that one of ordinary skill in the art would not have expected to have epothilone produced in a non-S.

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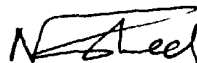
*cellulosum* presumably because of the lack of the appropriate methyltransferase, applicants should be reminded by the fact that none methylated epothilone, and epothilone A, B, C, and D among many others are considered epothilone D derivatives. It is possible that one of ordinary skill in the art may have not expected the same derivatives obtained by the applicants, but he/she would have expected other epothilone D derivatives. The prior art teach the epoD PKS, and modification of the  $\beta$ -keto group modifying activity result in the formation of new chemical compound belong to a class of compounds that are known to have anticancer and fungal activities. The ordinary skill in the art would have had the skills and the expectation of success. Thus, the claims remain rejected.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.  
Primary Examiner  
Art Unit 1652